

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (currently amended) A method of producing a substance or mixture for use in spheroid formation, the method comprising heat treatment of Fetal Calf Serum for a time and at a temperature sufficient to impart spheroid-forming activity to the resultant substance or mixture wherein the heat treatment is performed at a temperature between 60°C and 80°C for between 30 minutes and 12 hours.

2. (canceled)

3. (currently amended) [[A]] The method according to Claim 1, wherein the heat treatment is performed at a temperature between 65°C and 75°C.

4. (canceled)

5. (currently amended) [[A]] The method according to Claim 1, wherein the heat treatment is performed at a temperature of 70°C for about five hours.

6. (currently amended) [[A]] The method according to Claim 1, further comprising the step of storing the resultant substance or mixture in aliquots at about -20°C.

7. (previously presented) A substance or mixture for use in spheroid preparation formed by the method according to Claim 1.

8. (previously presented) A method of spheroid formation comprising contacting in a vessel a cell culture with a substance or mixture formed by the method of Claim 1.

9. (currently amended) [[A]] The method according to Claim 8, wherein the spheroid-forming substance or mixture is coated on the vessel.

10. (currently amended) [[A]] The method according to Claim 8, wherein a 5 to 10% solution of the spheroid-forming substance or mixture is added to a medium of the cell culture.

11. (currently amended) [[A]] The method according to Claim 8, wherein the cell culture comprises more than one cell type, whereby a hetero-spheroid is formed.

12. (withdrawn - currently amended) An elongate spheroid, ~~formed using the substance or mixture of claim 7,~~ produced by a method according to claim 8, said elongate spheroid comprising a plurality of cells arranged linearly.

13. (withdrawn - currently amended) [[An]] The elongate spheroid according to Claim 12 which has a length of at least 1cm.

14. (withdrawn - currently amended) [[An]] The elongate spheroid according to Claim 12, which contains 100,000- 200,000 cells per cm length.

15. (withdrawn - currently amended) [[An]] The elongate spheroid according to Claim 12, comprising more than one cell type.

16. (withdrawn - currently amended) [[An]] The elongate hetero-spheroid according to Claim 12, comprising an elongate core of cells of one type with one or more layers of cells of a different type arranged around said core.

17. (withdrawn - original) An elongate hetero-spheroid comprising MCF7 and breast fibroblast cells.

18. (withdrawn - currently amended) A method of forming an elongate spheroid comprising forming a suspension by contacting a cell culture with a spheroid-forming substance or mixture according to claim 4 at the required concentration, placing the suspension in a tubular member, incubating the contents of the tubular member, and removing the elongate spheroid.

19. (withdrawn - currently amended) [[A]] The method according to Claim 18, wherein the required concentration is in the range of 6 to 10 million cells/ml.

20. (withdrawn - currently amended) [[A]] The method according to Claim 18, wherein the tubular member has an internal diameter of about 1mm.

21. (withdrawn - currently amended) [[A]] The method according to Claim 18, further comprising the step of stretching the tubular member prior to the incubation.

22. (withdrawn - currently amended) A kit for forming elongate spheroids comprising a spheroid forming substance or mixture according to claim 7 and a tubular member.

23. (currently amended) ~~The use of~~ A method for producing a spheroid of cancer cells, comprising adding to a culture of cancer cells an effective amount of a spheroid-forming substance or mixture formed by the method of Claim 1 in anti-cancer therapy.

24. (original) A polymeric protein comprising a polymer of one or more proteins contained in fetal calf serum, having a molecular weight in excess of 2MDa and having spheroid forming activity.

25. (original) A polymeric protein obtainable by heat treatment of fetal calf serum, whereby said polymeric protein is capable of spheroid forming activity.

26. (currently amended) ~~The use of a polymeric protein according to Claim 24~~ A method for the production of spheroids for tissue culture comprising adding an effective amount of a polymeric protein to a culture of tissue cells.

27. (currently amended) ~~The use of a polymeric protein according to Claim 24~~ A method for the production of spheroids made up of one or more of fibroblasts, smooth muscle cells and bladder cancer cells, comprising adding to a culture of fibroblasts, smooth muscle cells, bladder cancer cells an effective amount of a protein according to claim 24.

28. (currently amended) ~~The use of a polymeric protein according to Claim 24~~ A method for the preparation of skin cells selected from the group comprising keratinocytes and fibroblasts,

for use in wound healing and/or skin grafting comprising adding to a culture of keratinocytes and fibroblasts an effective amount of a polymeric protein according to claim 24.

29. (withdrawn - previously presented) A method of elongate spheroid formation, which comprises providing an elongate culture vessel having a generally V-shaped lower cross-section, introducing into said culture vessel a cell culture and a spheroid-forming substance or mixture according to claim 7, incubating the contents of said vessel and removing the elongate spheroid.

30. (withdrawn - original) A method of producing a spheroid making up a grid structure, which comprises providing a corresponding culture vessel defining a grid in which the grid elements are of V-section, and introducing into said culture vessel a cell culture and a spheroid-forming substance or mixture, incubating the contents of said vessel and removing a spheroid of grid-like structure.

31. (withdrawn - previously presented) A method according to Claim 29, wherein said incubation is for a period of 24 to 36 hours.

32. (withdrawn - previously presented) A method according to Claim 29, wherein said V-shaped section defines an inclined angle in the range of from 20° to 120°.

33. (withdrawn - original) A kit for forming elongate spheroids or a grid-like structure thereof, comprising a

culture vessel having an elongate portion with a generally V-shaped lower cross-section, and a spheroid-forming substance or mixture.

34. (previously presented) A method of spheroid formation comprising contacting in a vessel one or more cell cultures with a polymeric protein according to Claim 24.

35. (new) The polymeric protein according to claim 24, wherein said polymeric protein is produced by heat treatment of fetal calf serum for a time and at a temperature sufficient to impart a spheroid-forming activity and wherein the heat treatment is performed at a temperature between 60°C and 80°C for between 30 minutes and 12 hours.